On the merits, claims 5 and 9 have been rejected as being anticipated under 35 U.S.C. 102(a) by Accession number U79958 of October 6, 1997. The present application is based upon a PCT application number PCT/EP98/05738 filed 9/9/98 which claims priority of German Application 197 396 11.9 filed September 9, 1997 which is earlier than the date of the Accession. Accordingly, it is unclear that this is prior art to the present invention, since under 35 U.S.C. 104, Applicants' filing in Germany (a WTO member country) in September 1997 *prima facie* establishes a date of invention prior to this reference. If Applicants' are incorrect in this regard, they would like the opportunity to comment on this reference.

Claims 5 and 9 have also been rejected under 35 U.S.C. 102(b) as anticipated by Accession No. Y00432 dated March 19, 1991 or Accession No. X15400, Nature 340 (1989) 531-536. Applicants provide the following comments in this regard.

While SEQ ID No. 2 is comprised by the known sequence of the 23S rDNA-gene, this does, however, not mean that it provides for a claim directed toward a kit comprising SEQ ID No. 2 as recited now in claim 11.

As to Accession No. X15400, the known oligonucleotide differs from SEQ ID No. 3 in positions 2 and 11. This means that SEQ ID No. 3 and any other oligonucleotide with a homology of at least 19 of 20 nucleotides compared to SEQ ID No. 3 is distinct therefrom.

Turning now to the rejection of claims 1-11 under 35 U.S.C. 103(a), the following comments regarding the references cited are provided. As to Kur et al. = Acta Microbiologica Polonica, 44 (1995) 111 - 117, the technique does not correspond to the standard of modern PCR technique. The described method is a combination of PCR and a restriction analysis. This method is relatively complicated and time-consuming and requires a gel electrophoresis. The restriction analysis requires specific restriction enzymes which result in characteristic lane patterns of the digested DNA. A comparison with the claimed invention would merely be possible in combination with specific primers. Thus, it is impossible to forecast any other DNA-target region for a PCR with primers still to be elected or conceived and with the mentioned enzyme for any analytical application.

Kur et al. suggest a PCR amplification of a DNA-

region designated as 16S-23S-spacer. This region is not identical with the target region of the present invention used for PCR-primers and probes; i.e. the 23S-5S intergenic region. There is no suggestion or motivation to make use of the target region of the application in question. Kur et al. does not suggest any primer or probe of this region. Further, any experimental or literal suggestion is missing which points to any other region than the 16S-23S-spacer for a detection of Pseudomonas.

In addition, according to Kur et al. page 114, legend for Fig. 1, the 16S-23S-spacer region is variable since the number of tRNAs, inserted into this region, is variable. Such a variability is, however, extremely disadvantageous for a species- or genus-specific analysis, since the presence of a differing number of tRNA-copies leads inevitably to variable results. In other words, a skilled worker in the art would avoid any use of this spacer region.

As to Jannes et al. = WO 96/00 298, in analogy to Kur et al., this art aims at use of the 16S-23S-spacer region. Jannes et al. mention primers and probes of the mentioned region for an amplification of rDNA and an detection of different species of bacteria. The teaching

of the present invention does not make any use of the 16S-23S-rDNA-spacer region.

Jannes et al. table 2 give examples for detection of Pseudomonas aeruginosa. It can be seen, that this species could be detected, but not any of the remaining species of the genus. In view of these results, a skilled worker in the art interested in a detection system for the genus Pseudomonas would hesitate to make any use of the 16S-23S-rDNA-spacer region.

As to U.S. Patent No. 5,714,321 to Hogan, table 44 thereof shows a detection of Pseudomonas species. This detection is based on probes which are derived from a specific conserved region of the 23S-rDNA; cf. col. 43 line 60. From the results can be drawn that the probe used by Hogan cannot detect all species of the genus Pseudomonas; cf. col. 44 line 24. This does not suggest to a skilled worker how to find useful primers or probes.

In summary, the present invention is unobvious, since a region has been identified which is not used by the references. This region is superior as regards specificity and detection potential since it lacks any of the mentioned drawbacks. Thus, SEQ ID No. 1 does not contain tRNAs. The region of SEQ ID No. 1 leads to an

election of oligonucleotides SEQ ID No. 3 to 5, which are suitable for a detection of Pseudomonas, also in combination with SEQ ID No. 2. Reference is made to example 1 and its table.

Accordingly, it is respectfully submitted that the present invention as now claimed is patentably distinct from the art cited taken alone or in combination. A notice of allowance is therefore earnestly solicited.

The Commissioner is authorized to charge any additional fees that may be required to Deposit Account No. 501145, Order No. 2727-102.

Respectfully submitted,

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APPENDIX:

3. (Amended) A nucleic [Nucleic] acid molecule having a shortened sequence compared with a nucleic acid molecule of SEQ ID No. 1 that being either [according to claim 1, namely]

(i) SEQ ID NO 3 or

(ii) SEQ ID NO 4 or

(iii) SEQ ID NO 5 or

(iv) the sequence complementary to each of (i), (ii) and (iii).

5. (Amended) A nucleic [Nucleic] acid molecule which [characterised in that], in respect of its sequence in at least 10 successive nucleotides of its nucleotide chain,

(i) [it] is identical to a nucleic acid molecule according to claim 3 [one of the preceding claims] or

(ii) [it] corresponds to a nucleic acid molecule according to claim 3 [one of the preceding claims] in 9 out of 10 successive nucleotides or

(iii) [it] corresponds to a nucleic acid molecule according to claim 3 [one of the preceding claims] in 8 out of 10 successive nucleotides or

(iv) it is at least 90 % homologous to a nucleic acid molecule according to claim 3 [one of the preceding claims], the

nucleic acid molecule allowing the detection of bacteria of the *Pseudomonas* genus.

6. (Amended) A nucleic [Nucleic] acid molecule according to claim 5, wherein the nucleic acid molecule [characterised in that it] is from 10 to 250, and preferably from 15 to 30, nucleotides long.

7. (Twice Amended) A nucleic [Nucleic] acid molecule according to claim 3 [1], wherein the nucleic acid molecule [characterised in that it] is single-stranded or double-stranded.

8. (Twice Amended) A nucleic [Nucleic] acid molecule according to claim 3 [1], wherein the nucleic acid molecule [characterised in that it] is present

(i) as DNA or

(ii) as RNA corresponding to (i) or

(iii) as PNA,

the nucleic acid molecule where appropriate having been modified in a manner known *per se* for analytical

detection processes, especially those based on hybridisation and/or amplification.

9. (Amended) A nucleic [Nucleic] acid molecule according to claim 8, wherein [characterised in that] the nucleic acid molecule has been modified in such a manner that up to 20 % of the nucleotides of at least 10 successive nucleotides of its nucleotide chain, especially 1 or 2 nucleotides, have been replaced by analogous building blocks known *per se* as probes [and/]or primers[, especially by nucleotides that do not occur naturally in bacteria].

10. (Twice Amended) A nucleic [Nucleic] acid molecule according to claim 8, wherein [characterised in that] the nucleic acid molecule has been modified or labelled or additionally modified or labelled in such a manner that it comprises, in a manner known *per se* for analytical detection processes, one or more radioactive groups, coloured groups, fluorescent groups, groups for immobilisation on a solid phase [and/]or groups for an indirect or direct reaction, [especially for an enzymatic reaction, preferably using antibodies, antigens, enzymes

and/or substances having an affinity for enzymes or enzyme complexes, and/]or otherwise modifying or modified groups of nucleic-acid-like structure.

11. (Twice Amended) A kit comprised of one [One] or more nucleic acid molecules selected from the group consisting of a nucleic acid molecule according to claim 3, nucleic acid molecule to SEQ ID No. 1 and nucleic acid molecule of SEQ ID No. 2 [according to claim 1] in the presence of optional auxiliary substances [and in the form of a kit] for analytical detection processes[, especially for the detection of bacteria of the *Pseudomonas* genus].

12. (Twice Amended) A method of detecting the presence or absence of bacteria comprising the step of using [Use of one or more nucleic acid molecules according to claim 1 or in the form of] a kit according to claim 11 for detection of the presence or absence of bacteria belonging to a group of bacteria of the *Pseudomonas* genus.

13. (Amended) The method [Use] according to claim 12, wherein [characterised in that] the group of bacteria of

the *Pseudomonas* genus includes various strains of *Pseudomonas aeruginosa* or is made up from those strains.

14. (Amended) The method [Use] according to claim 13, wherein [characterised in that] the group of bacteria of the *Pseudomonas* genus is composed exclusively of *Pseudomonas aeruginosa* strains.

15. (Twice Amended) The method [Use] according to claim 12, wherein [characterised in that] nucleic acid hybridisation [and/]or nucleic acid amplification or nucleic acid hybridization plus amplification [is/]are carried out.

16. (Amended) The method [Use] according to claim 15, wherein [characterised in that], as nucleic acid amplification, a polymerase chain reaction is carried out.

17. (Twice Amended) The method [Use] according to claim 12, wherein [characterised in that] the detection is carried out by distinguishing the to-be-detected bacteria from not-to-be-detected bacteria on the basis of

differences in the genomic DNA [and/]or RNA at at least one nucleotide position in the region of a nucleic acid molecule according to claim 3 [one of claims 1 to 10].

APPENDIX (CONT.)

--19. (New) A nucleic acid molecule according to claim 6, wherein the nucleic acid molecule is from 15 to 30, nucleotides long.

20. (New) A nucleic acid molecule according to claim 8, wherein the nucleic acid molecule is present

(i) as DNA or

(ii) as RNA corresponding to (i) or

(iii) as PNA,

the nucleic acid molecule where appropriate having been modified in a manner known *per se* for analytical detection processes based on hybridisation or amplification.

21. (New) A nucleic acid molecule according to claim 3, wherein the nucleic acid molecule has been modified in such a manner that 1 or 2 of the nucleotides of at least 10 successive nucleotides of its nucleotide chain have been replaced by analogous building blocks known *per se* as probes or primers.

22. (New). A nucleic acid molecule according to claim 3, wherein the nucleic acid molecule has been modified in such a manner that up to 20 % of the nucleotides of at least 10 successive nucleotides of its nucleotide chain have been replaced by nucleotides that do not occur naturally in bacteria.

23. (New) A nucleic acid molecule according to claim 10, wherein the nucleic acid molecule has been modified or labelled or additionally modified or labelled in such a manner that it comprises, in a manner known *per se* for analytical detection processes, one or more radioactive groups, coloured groups, fluorescent groups, groups for immobilisation on a solid phase or groups for an indirect or direct enzymatic reaction.

24. (New) A nucleic acid molecule according to claim 10, wherein the nucleic acid molecule has been modified or labelled or additionally modified or labelled in such a manner that it comprises, in a manner known *per se* for analytical detection processes, one or more groups for an indirect or direct reaction using antibodies, antigens,

enzymes or substances having an affinity for enzymes or enzyme complexes.

25. (New) A kit according to claim 11 for the detection of bacteria of the *Pseudomonas* genus.--

In claim 15, line 1, kindly delete "one of claims 12 to 14" and substitute therefor --claim 12--;

In claim 17, line 1, kindly delete "one of claims 12 to 16" and substitute therefor --claim 12--.

REMARKS

The claims of the above-identified application (the claims as amended under Article 34 of the PCT) have been amended to remove all multiple dependencies. No new matter has been added. Accordingly, an early examination of the application is respectfully requested.

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